Figure 1

Structure of VH do	main of	human	A6	antibody.
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1 GAG. E	2 GTC V	3 CAG Q			6 GAG E	TCT			10 GGC G	11 TTA L	12 GTC V	13 CAG Q	14 CCT P
15 GGG G	16 GGĠ G	17 TCC S	18 CTG L		20 CTC L		22 TGT C	23 TCA S	24 GCC A	25 TCT S	26 GGA G	27 TTC F	28 ACC T
29 TTC F	30 AGT S	AGC	TAT Y	GCT	34 ATG M	CAC	TGG			39 CAG Q		41 CCA P	42 GGG G
43.	44	45	46	47	48	49	50	51	52		53 5		
AAG	GGA	CTG	GAA	TAT	GTT	TCA	GCT.	A.II.	AGT.	AGT	TAA	GGG	GGI
K		L			v				S	S		<u>G</u>	
									S				
к 56	G 57	L 58	E 59	Y ·	V 61	s 62	A 63	I 64	S C	S DR2 66	N 67	G 68	G 69
K 56 AGC	G 57 ACA	L 58 TAC	E 59 TAC	Y 60 GCA	V 61 GAC	s 62 TCC	A 63 GTG	I 64 AAG	S 65 GGC	S DR2 66 AGA	67 TTC	G 68 ACC	G 69 ATC
к 56	G 57 ACA	L 58 TAC	E 59 TAC	Y 60 GCA	V 61	s 62 TCC	A 63 GTG	I 64 AAG	S 65 GGC	S DR2 66	N 67	G 68	G 69
K 56 AGC	G 57 ACA	L 58 TAC	E 59 TAC	Y 60 GCA	V 61 GAC	s 62 TCC	A 63 GTG	I 64 AAG	S 65 GGC	S DR2 66 AGA	67 TTC	G 68 ACC	G 69 ATC
56 AGC S	G 57 ACA T 71	58 TAC Y	59 TAC Y	9 60 GCA A	V 61 GAC D	\$ 62 TCC \$	63 GTG V	64 AAG K	\$ C 65 GGC G 79	S DR2 66 AGA R	81	68 ACC T	G 69 ATC I
56 AGC S	G 57 ACA T 71 AGA	58 TAC Y 72 GAC	59 TAC Y 73 AAT	Y 60 GCA A 74 TCC	V 61 GAC D 75 AAG	S 62 TCC S 76 AAC	A 63 GTG V 77 ACT	64 AAG K 78 CTG	S 65 GGC G 79 TAT	DR2 66 AGA R 80 CTT	67 TTC F 81 CAA	68 ACC T 82 ATG	69 ATC I a AGC
56 AGC S	G 57 ACA T 71	58 TAC Y	59 TAC Y	Y 60 GCA A 74 TCC	V 61 GAC D 75 AAG	\$ 62 TCC \$	63 GTG V	64 AAG K	\$ C 65 GGC G 79	S DR2 66 AGA R	81	68 ACC T	G 69 ATC I
K 56 AGC S 70 TCC	G 57 ACA T 71 AGA	58 TAC Y 72 GAC	59 TAC Y 73 AAT	Y 60 GCA A 74 TCC	V 61 GAC D 75 AAG	S 62 TCC S 76 AAC	A 63 GTG V 77 ACT	64 AAG K 78 CTG	S 65 GGC G 79 TAT	DR2 66 AGA R 80 CTT	67 TTC F 81 CAA	68 ACC T 82 ATG	69 ATC I a AGC
K 56 AGC S 70 TCC S	G 57 ACA T 71 AGA R	58 TAC Y 72 GAC D	59 TAC Y 73 AAT N	9 60 GCA A 74 TCC S	V 61 GAC D 75 AAG K	5 62 TCC 5 76 AAC N	63 GTG V 77 ACT T	64 AAG K 78 CTG L	5 65 GGC G 79 TAT Y	DR2 66 AGA R 80 CTT L	67 TTC F 81 CAA Q	68 ACC T 82 ATG M	69 ATC I a AGC s
K 56 AGC S 70 TCC S	G 57 ACA T 71 AGA R	58 TAC Y 72 GAC D	59 TAC Y 73 AAT N	74 TCC S 85 GAG	V 61 GAC D 75 AAG K	\$ 62 TCC \$ 76 AAC N 87 ACG	63 GTG V 77 ACT T	78 CTG L	5 65 GGC G 79 TAT Y	DR2 66 AGA R 80 CTT L 91 TAC	67 TTC F 81 CAA Q 92 TGT	68 ACC T 82 ATG M	69 ATC I a AGC s

Figure 1 (continued)

95 96 97 98 99 100 a b c d e f g h
GAC AGG TTA AAA GTG GAG TAC TAT GAT AGT AGT GGT TAT TAC
D R L K V E Y Y D S S G Y Y

CDR3

i j k l m n o 101 102 103 104 105 105 107
GTT TCT CGG TTC GGT GCT TTT GAT ATC TGG GGC CAA GGG ACA
V S R F G A F D I W G Q G T

Figure 2

Structure of modified V_H domain of human A6 antibody showing substitutions at position 44, 45, 47, 93 and 94. The *NheI* site is underlined.

	2 GTC V	CAG	CTG	CAG	6 GAG E	TCT	GGG	GGA	10 GGC G	11 TTA L	12 GTC V	13 CAG Q	14 CCT P
15 GGG G	16 GGG G	17 TCC S	CTG	AGA	CTC	TCC	TGT	TCA	24 <u>GCT</u> A	<u>AGC</u>	26 GGA G	27 TTC F	28 ACC T
29 TTC F	30 AGT S	AGC	TAT Y	GCT	ATG	CAC	TGG	GTC	38 CGC R	CAG	GCT	41 CCA P	
43 AAG K	GAA	45 CGT R	GAA	GGT	GTT	TCA	GCT	ATT	52 AGT S	AGT	TAA	GGG	GGT
56 AGC <u>s</u>	ACA	TAC	TAC	GCA	GAC	TCC	GTG	AAG	65 GGC <u>G</u>	AGA	TTC	ACC	69 ATC I
TCC	71 AGA R	GAC	AAT	TCC	AAG	AAC	ACT	CTG	79 TAT Y	CTT	CAA	82 ATG M	a AGC S
b AGT S	CTG	AGA	GCT	85 GAG E	GAC	ACG	88 GCT A	GTG	90 TAT Y	TAC	TGT		

Figure 2 (continued)

95 96 97 98 99 100 a b c d e f g h
GAC AGG TTA AAA GTG GAG TAC TAT GAT AGT AGT GGT TAT TAC
D R L K V E Y Y D S S G Y Y

CDR3

i j k l m n o 101 102 103 104 105 105 107
GTT TCT CGG TTC GGT GCT TTT GAT ATC TGG GGC CAA GGG ACA
V S R F G A F D I W G Q G T

Structure of $V_{\rm H}$ domain of human A6 antibody. The mutated nucleotides spanning residues 7-48 to remove the recombination site are in bold and underlined.

1	2 GTC	3 C7 7	4 TT A	5 CAG	6 G	7 аст	8. GGT	·9 GGC	10 GGA	11 CTG		13 CAA	14 CCA
E		Q	L	Q	E	S	G	G	G	L	V	Q	P
15 <u>GGA</u> G	GGA	17. TCC S	CTG	AGA	20 CTC L	TCC	TGT	TCA	24 GCC A	25 TCT S	GGA	TTC	28 ACC T
29 TTC F	AGT	AGC	TAT	GCT	ATG	CAC	TGG	GTC	CGC	CAG	GCT	41 CCA P	GGG
			C	DR1									
43 AAG K	44 GGA G	CTG	GAA	TAT	GTT	TCA	GCT	TTA	AGT	AGT	TAA	GGG G	GGT
				٠					C	DR2			•
AGC	57 ACA T	TAC	TAC	GCA	GAC	TCC	GTG	AAG	GGC	AGA	TTC	ACC	ATC
•												٠	
TCC	71 AGA R	GAC	TAA	TCC	AAG	AAC	ACT	CTG	TAT	CTT	CAA	ATG	a AGC S
b AGT S	c CTG L	AGA	GCT	GAG	GAC	ACG	GCT	GTG	TAT	TAC	TGT	93 GTG V	AAA

Figure 3 (continued)

95 96 97 98 99 100 a b c d e f g h
GAC AGG TTA AAA GTG GAG TAC TAT GAT AGT AGT GGT TAT TAC
D R L K V E Y Y D S S G Y Y

CDR3

i j k l m n o 101 102 103 104 105 105 107
GTT TCT CGG TTC GGT GCT TTT GAT ATC TGG GGC CAA GGG ACA

G

Q G

R F G A F D I W

Structure of modified V_H domain of human A6 antibody showing substitutions at position 44, 45, 47, 93 and 94. The mutated nucleotides spanning residues 7-48 to remove the recombination site as well as the NheI site are in bold and underlined.

1	2	3	4	5 CAC	6 CAA	7 .	8 GGT	9 GGC	10 GGA	11 CTG	12 GT G		14 CCA
GAG E		O	L L	O	E	S	G	G	G	L	V	Q	P
	·			~									
15	16	17	18	19	20	21	22	23	24	25			28
GGA	GGA	TCC	CTG	AGA	CTC	TCC	TGT,	TCA	GCT	AGC	GGA	TTC.	ACC
G	G	S	\mathbf{L}	R	L	S	С	S	Α	S	G	F	\mathbf{T}
							•						
20	3.0	21	32	33	.34	35	36	37	3.8	39	40	41	42
ውምር ማጥር	AGT	AGC	TAT	GCT	ATG	CAC	TGG	GTC	CGC	CAG	GCT	CCA	GGG
F	S	S ·	Y	Α	M	H	W	V	R ·	Q	A	P	G
	_		. (•							
						•						- 4 -	
43	44	45	46	47	48	49	50	51	52		53 5		
								A.II.	AGT S	AGT.	AAT.	C	GGT
K	E	R	E	G	V	S			<u>S</u>		11/	<u>G</u>	
				•	•					٠,٢٠٢			
56	57	58	59	60	6İ	62	63	64	65	66	.67	68	69
AGC	ACA	TAC	TAC	GCA	GAC	TCC	GTG	AAG	GGC	AGA	TTC	ACC	ATC
S	Т	<u>Y</u>	Y	Α	_D	<u>S</u>	V	Κ	G	R	F	${f T}$	Ι
	•								•				
70	71	72	73	. 74	75	76	77	78	79	80	81	82	a
70 TCC	71 AGA	72 GAC	73 AAT	74 TCC	75 AAG	76 AAC	77 ACT	78 CTG	79 TAT	80 CTT	81 CAA		

 \mathbf{T}

N

K

S

· R

D

N

L

Y

 \mathbf{L}

Figure 4 (continued)

87 88 89 90 91 92 93 94 85 86 83 84 b c AGT CTG AGA GCT GAG GAC ACG GCT GTG TAT TAC TGT GCA GCA V C \mathbf{T} Α Y Y Α E D R d e £ 99. 100 a b c 97 98 95 96 GAC AGG TTA AAA GTG GAG TAC TAT GAT AGT AGT TAT TAC Y Y D S <u>V</u> . E CDR3 101 102 103 104 105 105 107 0 k 1 m n GTT TCT CGG TTC GGT GCT TTT GAT ATC TGG GGC CAA GGG ACA \mathbf{T} F D I W G Q F · G A 108 109 110 111 112 113 ACG GTC ACC GTC TCA TCA T V T V S

kDa	1
209 124	
80	
49.1	t Logic (Angle)
34.8	क्षेत्रीय (अ.१४५) व स्टूब
28.9	
20.6	
7 1	and the same of th

2

Figure 6

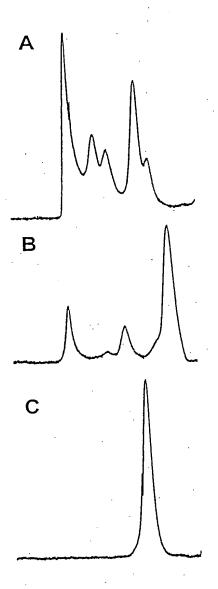
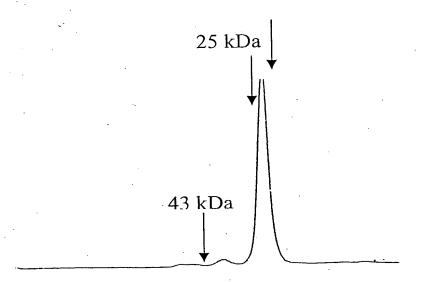
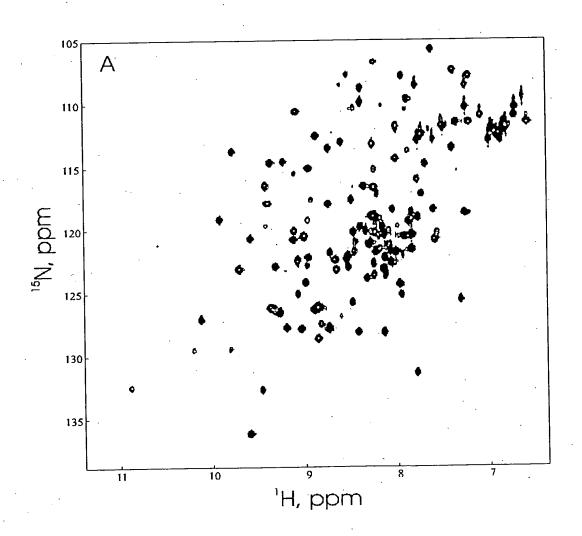


Figure 7



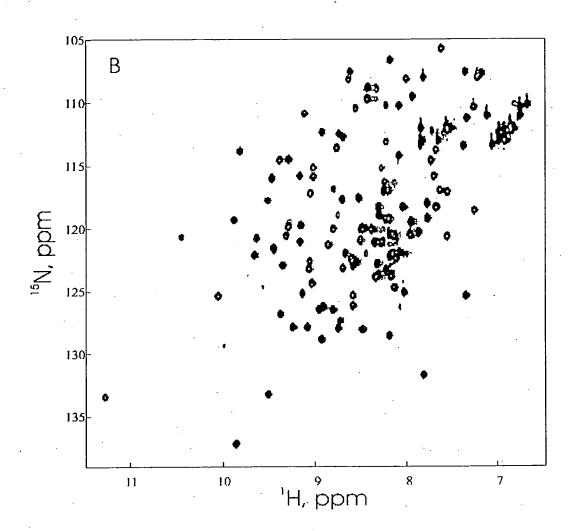
12/22

Figure 8A



13/22

Figure 8B



14/22

A6VH

Fr1	CDR1	Fr2	CDR2	Fr3		CDR3	Fr4
The second of	THE PROPERTY OF	The state of the state of	Section and the	and the effective	*** . * ** **	PRINCIPAL STATES	\$ di .
	A33	G44 L45 Y47			V93 K94	S100E	

<u>A6VH.1</u>



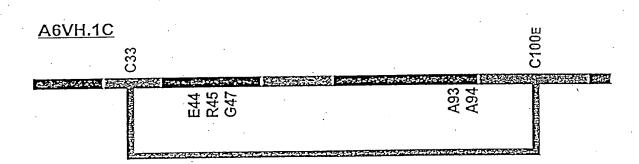


Figure 10

Structure of modified VH domain of human A6 antibody showing substitutions at position 33, 44, 45, 47, 93, 94 and 100e.

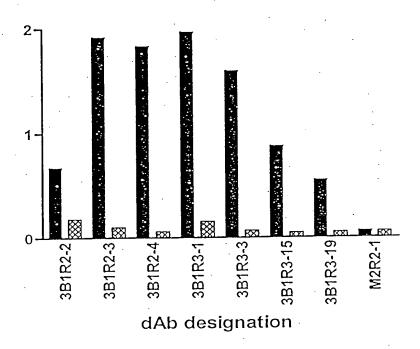
1 GAG E	2 GTC V	3 CAG Q		CAG	6 GAG E		GGG		10 GGC G	11 TTA L		13 CAG Q	14 CCT P
15 GGG G	16 GGG G	17 TCC S	18 CTĢ L	AGA		TCC	TGT		24 GCC A	25 TCT S		27 TTC F	28 ACC T
29 TTC F	30 AGT S	31 AGC S	TAT	TGT	ATG	35 CAC <u>H</u>	TGG	37 GTC V	38 CGC R	39 CAG Q	GCT	41 CCA P	42 GGG G
				DR1									
43 AAG K		CGT		GGT	GTT		GCT	TTA	52 AGT S		AAT		GGT
AGC	ACA	TAC	TAC	GCA	61 GAC D	TCC	GTG	ĄAG	65 GGC <u>G</u>	66 AGA R		68 ACC T	
70 TCC S	71 AGÁ R	72 GAC D	73 AAT N	TCC	75 AAG K	AAC	ACT	CTG	79 TAT Y	80 CTT L	81 CAA Q		
b AGT S	c CTG L		GCT		86 GAC D		GCT			91 TAC Y		93 GCA A	94 GCA A

Figure 10 (continued)

GAC	AGG	TTA	AAA	GTG	100 GAG E	TAC	TAT	GAT	AGT	TGC	GGT		
							R3			-			
GTT	TCT	CGG	TTC	GGT	n GCT A	TTT	GAT	ATC	TGG	GGC	CAA	105 GGG G	ACA
ACG		ACC	GTC	112 TCA	TCA							٠	

1,7/22

Figure 11

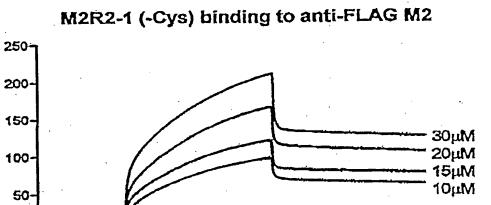


500

400

18/22

Figure 12



300

Time (sec)

200

Response (RU)

0-

-50-|-

100

Figure 13

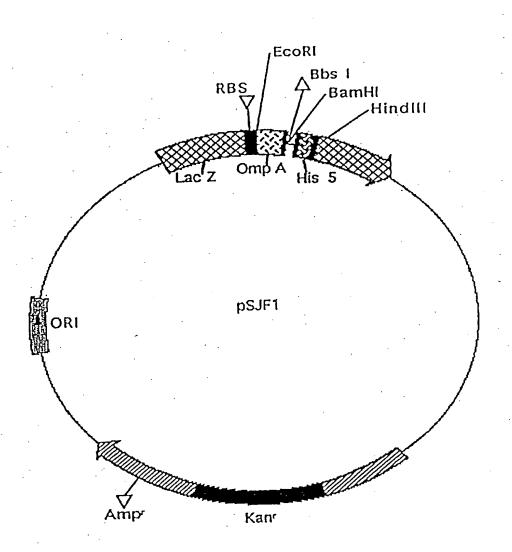


Figure 14

Structure of $V_{\rm H}$ domain of human A6 antibody. The mutated nucleotides spanning residues 7-48 to remove the recombination site are in bold and underlined.

1			4								12	13	14
											GTG		
E	`V	Q	L	Q	E	S	G	G	G	L	V	Q	. P
			.	7.0	0.0		22	2.2	2.4	2.5	26	0.7	2.0
15						21						27	28
											GGA		ACC
G	·G	S	L	R	ட	S	C	S	Α	S	G	F	\mathbf{T}_{i}
20	20	21	2.2		24	2 E	26	27	20	20	40	4 1	12
2 9 TTTC	30	2 T	ייט עייט ביי עייט		y un.⊂. ⊃i.æ	CVC	TCC	CTC	CGC	CNC	GCT	ÇCV I I	GGG
											A		
r _.	۵	<u>s</u>		DR1			**	V	IC .	Q.	A	<i>E</i>	G
				DKT									
43	44	45	46	4.7	48	49	.50	51	52	a 5	53 5	54 5	55
											TAA		
					V	S	<u>A</u>	I	S	S	N	G	
					V	S	<u>A</u>	I		S DR2	N	G ;	
K	G	L .	E	Y ·					C	DR2			<u>G</u>
K 56	G 57	L .	E 59	Y .	61	62	63	64	C 65	DR2	67	68	G 69
K 56	G 57 ACA	L 58 TAC	E 59 TAC	Y 60 GCA	61 GAC	62 TCC	63 GTG	64 AAG	C 65 GGC	DR2 66 AGA	67 TTC	68 ACC	G 69
K 56	G 57 ACA	L 58 TAC	E 59 TAC	Y 60 GCA	61 GAC	62 TCC	63 GTG	64 AAG	C 65 GGC	DR2 66 AGA	67	68 ACC	G 69
K 56 AGC	G 57 ACA	L 58 TAC	E 59 TAC	Y 60 GCA	61 GAC	62 TCC	63 GTG	64 AAG	C 65 GGC	DR2 66 AGA	67 TTC	68 ACC	G 69 ATC
K 56 AGC <u>S</u>	G 57 ACA T	L 58 TAC Y	E 59 TAC Y	Y 60 GCA A	61 GAC D	62 TCC S	63 GTG V	64 AAG K	C 65 GGC <u>G</u>	DR2 66 AGA R	67 TTC F	68 ACC T	G 69 ATC I
K 56 AGC S	G 57 ACA T	58 TAC Y	59 TAC Y	9 60 GCA A 74	61 GAC D	62 TCC S	63 GTG V	64 AAG K 78	65 GGC <u>G</u>	DR2 66 AGA R	67 TTC F	68 ACC T	G 69 ATC I
K 56 AGC S 70 TCC	G 57 ACA T 71 AGA	58 TAC Y 72 GAC	59 TAC Y 73 AAT	Y 60 GCA A 74 TCC	61 GAC D 75 AAG	62 TCC S 76 AAC	63 GTG V 77 ACT	64 AAG K 78 CTG	65 GGC G 79 TAT	DR2 66 AGA R 80 CTT	67 TTC F 81 CAA	68 ACC T - 82 ATG	G 69 ATC I a AGC
K 56 AGC S 70 TCC	G 57 ACA T 71 AGA	58 TAC Y 72 GAC	59 TAC Y 73 AAT	Y 60 GCA A 74 TCC	61 GAC D 75 AAG	62 TCC S	63 GTG V 77 ACT	64 AAG K 78 CTG	65 GGC <u>G</u>	DR2 66 AGA R 80 CTT	67 TTC F	68 ACC T	G 69 ATC I
K 56 AGC S 70 TCC	G 57 ACA T 71 AGA	58 TAC Y 72 GAC	59 TAC Y 73 AAT	Y 60 GCA A 74 TCC	61 GAC D 75 AAG	62 TCC S 76 AAC	63 GTG V 77 ACT	64 AAG K 78 CTG	65 GGC G 79 TAT	DR2 66 AGA R 80 CTT	67 TTC F 81 CAA	68 ACC T - 82 ATG	G 69 ATC I a AGC
K 56 AGC S 70 TCC S	G 57 ACA T 71 AGA R	58 TAC Y 72 GAC D	E 59 TAC Y 73 AAT N	Y 60 GCA A 74 TCC S	61 GAC D 75 AAG K	62 TCC S 76 AAC N	63 GTG V 77 ACT T	64 AAG K 78 CTG L	65 GGC G 79 TAT Y	DR2 66 AGA R 80 CTT L	67 TTC F 81 CAA Q	68 ACC T 82 ATG M	G 69 ATC I a AGC S
K 56 AGC S 70 TCC S	G 57 ACA T 71 AGA R	58 TAC Y 72 GAC D	59 TAC Y 73 AAT N	Y 60 GCA A 74 TCC S	61 GAC D 75 AAG K	62 TCC S 76 AAC N	63 GTG V 77 ACT T	64 AAG K 78 CTG L	65 GGC G 79 TAT Y	DR2 66 AGA R 80 CTT L	67 TTC F 81 CAA Q	68 ACC T - 82 ATG M	G 69 ATC I a AGC S
K 56 AGC S 70 TCC S b AGT	G 57 ACA T 71 AGA R	58 TAC Y 72 GAC D 83 AGA	E 59 TAC Y 73 AAT N 84 GCT	Y 60 GCA A 74 TCC S 85 GAG	61 GAC D 75 AAG K 86 GAC	62 TCC S 76 AAC N	63 GTG V 77 ACT T	64 AAG K 78 CTG L 89 GTG	65 GGC G 79 TAT Y	DR2 66 AGA R 80 CTT L 91 TAC	67 TTC F 81 CAA Q	68 ACC T - 82 ATG M	G 69 ATC I a AGC S

Figure 14 (contined)

GAC	AGG	TTA	AAA	GTG	GAG	TAC	TAT	GAT	d AGT S	AGT	GGT	TAT	TAC
						CI							
GTT	TCT	CGG	TTC	GGT	GCT	TTT	GAT	ATC		GGC	CAA	GGG	107 ACA

Figure 15

